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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/078,278	02/20/2002	Robert E. Wagner JR.	40011-178452	3427

30827 7590 12/09/2004

MCKENNA LONG & ALDRIDGE LLP
1900 K STREET, NW
WASHINGTON, DC 20006

EXAMINER	
BAUSCH, SARAE L	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/078,278	WAGNER ET AL.	
	Examiner	Art Unit	
	Sarae Bausch	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-55* is/are pending in the application.

4a) Of the above claim(s) *52- 55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/02, 06/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 29-51 in the reply filed on 09/29/2004 is acknowledged. The response provides no arguments with the traversal regarding the restriction requirement. It is noted that claims 52-55 have been withdrawn. The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 29-44 and 46-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kigawa et al (US Patent 5965361 Oct 1999) in view of Nolan et al. (WO 99/22029 May 1999).

Kigawa et al. teach a method for detecting the presence of a double stranded target nucleic acid sequence using a probe/RecA complex (abstract). Kigawa et al. teach the use of a nucleic acid probe, typically a single stranded nucleic acid prepared by a virus, plasmid, or a cosmid, a probe DNA moiety excised from a vector, or probe from an oligonucleotide synthesizing method (instant claim 32) (see column 5, lines 64-67 and column 6, lines 1-10). Kigawa et al. teach probes with 90-95% homology to the target nucleic acid sequence and a length of 100 to 1500 bases but longer or short polynucleotide probe may be used (instant claim 33) (see column 6, lines 12-18). Further, Kigawa et al. teach nucleotide probes with a label, such as a fluorescent indicator, a radioactive label or a ligand that can be bound to a specific reporter molecule such as biotin and digoxigenin (instant claim 34) (see column 6, lines 23-28). Kigawa et al. teach the use of RecA protein with a detectable label or ligand, such as a fluorescent indicator, a chemiluminscent agent, an enzymatic label, a radioactive label, biotin or digoxigenin (instant claim 35-36, 39 and 41) (see column 6, lines 61-67). Kigawa et al. teach alternatively detecting the double-stranded target nucleic acid by allowing the probe/RecA complex to react with an anti-RecA antibody with or without a label or ligand (instant claim 40) (see column 10, lines 50-58). Kigawa et al. teach the hybridization reaction can be performed in the presence of another protein, such as a single-stranded binding protein, if necessary to accelerate the reaction (instant claim 44) (see column 9, lines 18-22). Kigawa et al. teach detecting the presence of the double stranded target sequence by detecting a fluorescent signal derived from the RecA protein having a fluorescent label included in the probe/RecA complex bound to the target sequence detected with a fluorescent microscope or flow cytometer (instant claim 42-43

and 46) (see column 10, lines 24-32). Kigawa et al. teach the use of the probe/RecA hybridization method to detect various types of chromosomal aberration such as deletion and insertion (see column 13, lines 18-21). Kigawa et al. does not teach the use of MutS protein with RecA for the detection of chromosomal aberrations.

Nolan et al. teach a method of detection of DNA polymorphisms including nucleotide polymorphisms, insertions, and deletions (page 1, line 6-7) that includes using an immobilized mismatch-binding protein-coated microspheres to bind fluorescently labeled, mismatch-containing DNA by flow cytometry (instant claims 42-43, 46 and 48) (page 4, lines 24-26). Nolan et al. teach genomic DNA amplified by PCR using fluorescently labeled nucleotide triphosphates (instant claim 31, 32 and 47) (page 4, lines 26-28). Nolan et al. teach microspheres bearing immobilized mismatch-binding protein and further teach mismatch binding proteins to include bacterial mismatch-binding protein, MutS, or any other protein that recognizes DNA base pair mismatches which can be immobilized on microspheres by physical absorption or by the use of an affinity tag which binds to an affinity partner immobilized on microspheres, such as biotin affinity tag and avidin/streptavidin binding partner (instant claim 34 and 36-38, 49-51) (page 5, lines 23-29 and page 6 Table).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of detecting the double stranded target nucleic acid using a probe/RecA complex by Kigawa et al. to include the MutS protein detection system as taught by Nolan et al. to improve the method of probe/RecA detection system by Kigawa et al. The ordinary artisan would have been motivated to improve the method of detecting the double stranded target nucleic acid

sequence using the probe/RecA hybridization system by Kigawa et al. with the mismatch binding protein, MutS immobilized to microspheres taught by Nolan et al. because Nolan et al. teaches that the MutS immobilized detection system provides a high throughput, small volume, and washless method for detecting SNPs in DNA (page 4, lines 5-6). Further, the method of Nolan et al. allows for rapid scanning of mismatch DNA which would improve the detection of RecA/probe complex formation taught by Kigawa et al. The ordinary artisan would have had a reasonable expectation of success that the use of MutS could be used in the method by Kigawa et al. because Nolan et al. teach that the use of MutS immobilized onto microspheres for the detection of SNPs with flow cytometry provides multiparameter detection with excellent sensitivity in a homogenous assay format and multicolor fluorescent detection can be exploited for the simultaneous detection of dozens, or potentially hundred of analytes in a single sample (page 3, lines 9-14).

5. Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kigawa et al (US Patent 5965361 Oct 1999) in view of Nolan et al. (WO 99/22029 May 1999) as applied to claims 29-44 and 46-51 above in section 4, and further in view of Olson et al. (US Patent 5888728 March 1999).

The method of Kigawa et al. in view of Nolan et al. is set forth in section 4 above. Kigawa et al. in view of Nolan et al. does not teach the use of SSB protein labeled with a detectable label.

Olson et al. teach streptavidin bound to biotinylated SSB in order for the complex (SSB-oligonucleotide) to bind to a capture membrane (see column 5, lines 39-50 and 55-60).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of Kigawa et al. in view of Nolan et al. of detecting a mutation in a double stranded test DNA molecule with a probe/RecA complex bound to the test DNA and contacting the DNA with MutS protein to detect the presence of MutS bound to the DNA structure with SSB to include a labeled SSB protein as taught by Olson et al. to improve the detection of the mutation in the target DNA. The ordinary artisan would have been motivated to improve the method of Kigawa et al. in view of Nolan et al. to include a labeled SSB protein because Olson et al. teach that the assay can be performed with many combinations of sequential assays(see column 4, lines 36-39). Furthermore, Olson further teaches that many complexes may be formed and these complexes may have one or more components and the assay can be designed to avoid interference from specific substances (see column 4, lines 59-65), therefore the ordinary artisan would have had a reasonable expectation of success to include a labeled SSB, in the method of Kigawa et al. in view of Nolan et al.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571) 272-2912. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Jehanne Sitton
JEHANNE SITTON
PRIMARY EXAMINER
12/7/04

Sarae Bausch, PhD.
Examiner
Art Unit 1634